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Patricia K. Hines  
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

COUSENS et al.

Serial No.: CON of 08/449,070

Group Art Unit: Unassigned

Filing Date: Herewith

Examiner: Unassigned

Title: **EXPRESSION USING FUSED GENES PROVIDING FOR PROTEIN  
PRODUCT**

**BLANKET PETITION FOR EXTENSION OF TIME AND  
AUTHORIZATION TO CHARGE OR CREDIT DEPOSIT ACCOUNT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

If a paper is untimely filed in this application or any file wrapper continuation application derived therefrom by applicant(s) or her/his/their representative, the Commissioner is hereby petitioned under 37 C.F.R. § 1.136(a) for the minimum extension of time required to make said paper timely. In the event a petition for extension of time is made under the provisions of this paragraph, the Commissioner is hereby requested to charge any fee required under 37 C.F.R. § 1.17(a)-(d) to Deposit Account No. 18-1648. This, however, is not authorization to pay the issue fee.

If a paper is concurrently or subsequently filed in this application or any file wrapper continuation application derived therefrom by applicant(s) or her/his/their representative and a fee under 37 C.F.R. §§ 1.16-1.17 is required to effect any amendment, petition or other action requested in said paper, the Commissioner is hereby requested to charge any deficiency in said fee, or credit any overpayment of said fee, to Deposit Account No. 18-1648. This, however, is not authorization to pay the issue fee.

Respectfully submitted,

Date: 8/16/01

By: Roberta L. Robins  
Roberta L. Robins  
Registration No. 33,208

CHIRON CORPORATION  
Intellectual Property - R440  
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Telephone: (650) 325-7812  
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Atty Dkt No. PP00037.201  
2300-0037.04  
PATENT

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PATRICIA K. HEMMES  
Typed or Printed Name of Person Mailing Paper or Fee

Patricia K. Hemmes  
Signature of Person Mailing Paper or Fee

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

COUSENS et al.

Serial No.: CON of 08/449,070

Art Unit: Unassigned

Filing Date: herewith

Examiner: Unassigned

Title: EXPRESSION USING FUSED GENES PROVIDING FOR  
PROTEIN PRODUCT

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

This Amendment is filed with a Rule 1.53(b) application. Entry of the following amendments is requested prior to examination.

**I. AMENDMENTS**

**In the specification:**

On page 1, please replace the paragraph beginning on line 5 with the following:

--This application is a continuation of U.S. Serial No. 08/449,070, filed 24 May 1995, which is a continuation of U.S. Serial No. 08/088,566, filed 6 July 1993 which is a continuation-in-part of U.S. Serial No. 07/680,046, filed 29 March 1991, which is a continuation of application Serial No. 07/169,833, filed 17 March 1988, which is a continuation-in-part of U.S. Serial No. 717,209, filed 28 March 1985, from which priority is claimed pursuant to 35 U.S.C. § 120, and which applications are incorporated herein by reference in their entireties.--

**In the claims:**

Please cancel claims 1-17, without prejudice or disclaimer.

Please add new claims 18 to 23 as follows:

18. (New) A method for producing a heterologous polypeptide comprising
  - (a) introducing a DNA sequence coding for a fusion polypeptide comprising the heterologous polypeptide and superoxide dismutase into a host cell;
  - (b) culturing the host cell under conditions such that the fusion polypeptide is expressed; and
  - (c) isolating the fusion polypeptide from the host cell.
19. (New) The method of claim 18, wherein the host cell is a prokaryotic cell.
20. (New) The method of claim 19, wherein the prokaryotic host cell is *E. coli*.

21. (New) The method of claim 19, wherein the prokaryotic host cell is *B. subtilis*.

22. (New) The method of claim 20, wherein the heterologous polypeptide is a mammalian polypeptide.

23. (New) The method of claim 21, wherein the heterologous polypeptide is a mammalian polypeptide.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendments. The attached pages are captioned “**Version with markings to show changes made.**”

II. REMARKS

New claims 18-23 have been added and find support throughout the specification as filed, for example on page 3, lines 24-30. Entry of the amendments is respectfully requested. These amendments obviate all previous rejections. Applicants note that these amendments are made solely to advance prosecution and are not in any intended as an acknowledgment that the Examiner's position in the parent case was correct.

The Examiner is requested to direct all further communication in this application to:

Lisa M. Alexander  
Chiron Corporation  
Intellectual Property - R440  
P.O. Box 8097  
Emeryville, CA 94662-8097  
Telephone: (510) 923-2585  
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Respectfully submitted,

Date: Aug 16, 2001

By: Dahna S. Pasternak  
Dahna S. Pasternak  
Registration No. 41,411  
Attorney for Applicants

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**Version with markings to show changes made to claims**

1-17. Canceled.

18. (New) A method for producing a heterologous polypeptide comprising  
(a) introducing a DNA sequence coding for a fusion polypeptide comprising the heterologous polypeptide and superoxide dismutase into a host cell;  
(b) culturing the host cell under conditions such that the fusion polypeptide is expressed; and  
(c) isolating the fusion polypeptide from the host cell.

19. (New) The method of claim 18, wherein the host cell is a prokaryotic cell.

20. (New) The method of claim 19, wherein the prokaryotic host cell is *E. coli*.

21. (New) The method of claim 19, wherein the prokaryotic host cell is *B. subtilis*.

22. (New) The method of claim 20, wherein the heterologous polypeptide is a mammalian polypeptide.

23. (New) The method of claim 21, wherein the heterologous polypeptide is a mammalian polypeptide.

## VERSION SHOWING CHANGES MADE TO SPECIFICATION

CON OF USSN 08/449,070

Variable	Mean	Standard deviation	Minimum	Maximum
Age	34.5	10.5	20	55
Gender	0.5	0.5	0	1
Marital status	0.5	0.5	0	1
Education	12.5	1.5	10	15
Income	1.5	0.5	1	2
Health status	1.5	0.5	1	2
Smoking status	0.5	0.5	0	1
Alcohol consumption	0.5	0.5	0	1
Exercise frequency	1.5	0.5	1	2
Stress level	1.5	0.5	1	2
Sleep quality	1.5	0.5	1	2
Work satisfaction	1.5	0.5	1	2
Life satisfaction	1.5	0.5	1	2
Overall health	1.5	0.5	1	2
Physical activity	1.5	0.5	1	2
Mental health	1.5	0.5	1	2
Social support	1.5	0.5	1	2
Work-life balance	1.5	0.5	1	2
Financial stability	1.5	0.5	1	2
Family harmony	1.5	0.5	1	2
Personal growth	1.5	0.5	1	2
Community involvement	1.5	0.5	1	2
Environmental awareness	1.5	0.5	1	2
Cultural appreciation	1.5	0.5	1	2
Artistic expression	1.5	0.5	1	2
Volunteer work	1.5	0.5	1	2
Charitable contributions	1.5	0.5	1	2
Philanthropic activities	1.5	0.5	1	2
Leadership roles	1.5	0.5	1	2
Teamwork skills	1.5	0.5	1	2
Communication skills	1.5	0.5	1	2
Problem-solving abilities	1.5	0.5	1	2
Emotional resilience	1.5	0.5	1	2
Stress management	1.5	0.5	1	2
Time management	1.5	0.5	1	2
Organization skills	1.5	0.5	1	2
Attention to detail	1.5	0.5	1	2
Initiative taking	1.5	0.5	1	2
Adaptability	1.5	0.5	1	2
Resilience	1.5	0.5	1	2
Optimism	1.5	0.5	1	2
Empathy	1.5	0.5	1	2
Compassion	1.5	0.5	1	2
Kindness	1.5	0.5	1	2
Generosity	1.5	0.5	1	2
Humility	1.5	0.5	1	2
Patience	1.5	0.5	1	2
Forgiveness	1.5	0.5	1	2
Gratitude	1.5	0.5	1	2
Positivity	1.5	0.5	1	2
Enthusiasm	1.5	0.5	1	2
Passion	1.5	0.5	1	2
Dedication	1.5	0.5	1	2
Commitment	1.5	0.5	1	2
Responsibility	1.5	0.5	1	2
Accountability	1.5	0.5	1	2
Integrity	1.5	0.5	1	2
Honesty	1.5	0.5	1	2
Transparency	1.5	0.5	1	2
Openness	1.5	0.5	1	2
Flexibility	1.5	0.5	1	2
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Adaptability	1.5	0.5	1	2
Resilience				

IMPROVED EXPRESSION USING FUSED GENES  
PROVIDING FOR PROTEIN PRODUCT

CROSS-REFERENCE TO RELATED APPLICATIONS

5 This application is a continuation of U.S. Serial No. 08/449,070, filed 24 May 1995,  
which is a continuation of U.S. Serial No. 08/088,566, filed 6 July 1993 which is a continuation-  
in-part of U.S. Serial No. 07/680,046, filed 29 March 1991, which is a continuation of  
application Serial No. 07/169,833, filed 17 March 1988, which is a continuation-in-part of U.S.  
Serial No. 717,209, filed 28 March 1985, from which priority is claimed pursuant to 35 U.S.C. §  
10 120, and which applications are incorporated herein by reference in their entirety.

BACKGROUND OF THE INVENTION

Field of the Invention

15 There are an increasingly large number of genes available for expression, where the  
expression product may find commercial use. In many instances, the initial expression has been  
observed in *E. coli*. Expression in *E. coli* has many disadvantages, one in particular being the  
presence of an enterotoxin which may contaminate the product and make it unfit [to] for  
administration to mammals. Furthermore, there has not previously been an extensive technology  
concerned with the production of products in *E. coli*, as compared to such other microorganisms  
20 as *Bacillus subtilis*, *Streptomyces*, or yeast, such as *Saccharomyces*.

In many situations, for reasons which have not been resolved, heterologous products,  
despite active promoters and high copy number plasmids, are produced in only minor amount, if  
at all, in a microorganism host. Since the economics of the processes are dependent upon a



**SUBSTITUTE COPY OF PAGE 1 OF SPECIFICATION**

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